L47 ANSWER 3 OF 5 MEDLINE

ACCESSION NUMBER: 2000060325 MEDLINE

DOCUMENT NUMBER: 20060325

TITLE: [Treatment of multiple sclerosis. The present and the future. Study Group on Diagnosis and Therapy of Multiple

Sclerosis].

Il trattamento della sclerosi multipla. Il presente ed il futuro. Gruppo di Studio per la Diagnosi e Terapia della

Polisclerosi.

AUTHOR: Cazzato G; Antonello R M; Zorzon M; Torre P; Zivadinov R;

Moretti R; Bragadin L M; De Masi R; Nasuelli D

CORPORATE SOURCE: Istituto di Clinica Neurologica, Universit`a, Trieste..

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SOURCE: RECENTI PROGRESSI IN MEDICINA, (1999 Oct) 90 (10) 538-44.

Ref: 40

Journal code: RIT. ISSN: 0034-1193.

PUB. COUNTRY: Italy

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: Italian ENTRY MONTH: 200003 ENTRY WEEK: 20000302

The last years have produced a plethora of new information including extensive studies, retrospective analysis and new perspectives on data interpretation on multiple sclerosis (MS) treatment. Considering how difficult it is to study a disease such MS with its variability, unpredictability and duration, it seems hard to resemble definite results from this experience. However, corticosteroids have been the mainstay of treatment for the management of acute relapses, showing the capacity to shorten the duration of relapses, accelerate the recovery. At present, interferon beta is generally considered to be the treatment of choice for patients with relapsing remitting disease. Glatiramer acetate is still not available in many parts of Europe, but its results demonstrate

as alternative treatment the immunosuppressive drugs, chosen if patients demonstrate unacceptable side effects of interferon or clearly do not respond. Very different and even more confusing data still come from experimental trial in secondary progressive MS, where the target of treatment is to slow the progression of disability. Different drugs (methotrexate, mitoxantrone, linomide, steroids and even interferons) are employed, but the results are still debated. Future therapies are being derived from constantly changing and evolving concept of MS immunopathogenesis: therefore many experimental and clinical trials use anti-integrin antibodies or insulin growth factors, metallo-proteinase inhibitors or T-cell vaccination. Some of the above treatment may have a chance of producing the gaining control of the disease without much inner toxicity.

AB . . . recovery. At present, interferon beta is generally considered to be the treatment of choice for patients with relapsing remitting disease. Glatiramer acetate is still not available in many parts of Europe, but its results demonstrate a reduction of relapses in 30%. . . changing and evolving concept of MS immunopathogenesis: therefore many experimental and clinical trials use anti-integrin antibodies or insulin growth factors, metallo-proteinase inhibitors or T-cell vaccination. Some of the above treatment may have a chance of producing the gaining control of the disease. . .

Applicants: Alexander Gad and Dora Lis

Serial No.: 09/816,989 Filed: March 23, 2001

Exhibit 16

L47 ANSWER 3 OF 5 MEDLINE

ACCESSION NUMBER: 2000060325 MEDLINE

DOCUMENT NUMBER:

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Applicants: Adrian Gilbert et al.

Serial No.: 09/788,131 Filed: February 16, 2001

Exhibit 150

L47 ANSWER 3 OF 5 MEDLINE ACCESSION NUMBER: 2000060325

DOCUMENT NUMBER:

20060325

TITLE:

[Treatment of multiple sclerosis. The present and the future. Study Group on Diagnosis and Therapy of Multiple

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SOURCE:

RECENTI PROGRESSI IN MEDICINA, (1999 Oct) 90 (10) 538-44.

Ref: 40

Journal code: R1T. ISSN: 0034-1193.

MEDLINE

PUB. COUNTRY:

Italy

Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE:

Italian 200003

ENTRY MONTH: ENTRY WEEK:

20000302

The last years have produced a plethora of new information including extensive studies, retrospective analysis and new perspectives on data interpretation on multiple sclerosis (MS) treatment. Considering how difficult it is to study a disease such MS with its variability, unpredictability and duration, it seems hard to resemble definite results from this experience. However, corticosteroids have been the mainstay of treatment for the management of acute relapses, showing the capacity to shorten the duration of relapses, accelerate the recovery. At present, interferon beta is generally considered to be the treatment of choice for patients with relapsing remitting disease. Glatiramer acetate is still not available in many parts of Europe, but its results demonstrate

reduction of relapses in 30% of cases. Most European experts only consider

as alternative treatment the immunosuppressive drugs, chosen if patients demonstrate unacceptable side effects of interferon or clearly do not respond. Very different and even more confusing data still come from experimental trial in secondary progressive MS, where the target of treatment is to slow the progression of disability. Different drugs (methotrexate, mitoxantrone, linomide, steroids and even interferons) are employed, but the results are still debated. Future therapies are being derived from constantly changing and evolving concept of MS immunopathogenesis: therefore many experimental and clinical trials use anti-integrin antibodies or insulin growth factors, metalloproteinase inhibitors or T-cell vaccination. Some of the above treatment may have a chance of producing the gaining control of the disease without much inner toxicity.

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Applicants: Adrian Gilbert et al.

Serial No.: 09/788,131 Filed: February 16, 2001

Exhibit 150